REMARKS

The Office Action sent April 1, 2008 has been received and reviewed. All claims currently under consideration stand rejected. Applicants note with appreciation the withdrawal of the previous objections and rejections. All amendments are made without prejudice or disclaimer.

Support for the current amendments and new claim can be found throughout the Specification, for example, in paragraphs **[0040], [0056], [0085], [0087]-[0090],** and the claims as previously presented. Accordingly, applicants submit that no new matter has been added. Reconsideration is respectfully requested.

35 U.S.C § 103

Claims 1, 2, 7, and 12 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoeprich (of record) in view of Davila (US Patent 5,894,018) and further in view of Rodriquez et al. (US Patent 5,286,484). Applicants respectfully traverse the rejections.

"To establish obviousness the prior art itself or the inferences and creative steps that a person of ordinary skill in the art would [have] employ[ed]" at the time of the invention are to have taught or suggested all of the claim elements. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742, 167 L.Ed.2d 705, 75 USLW 4289, 82 USPQ2d 1385 (2007). Furthermore, to establish a *prima facie* case of obviousness there must have been a reasonable expectation of success. M.P.E.P. § 2143.02.

Applicants respectfully submit that claims 1, 2, 7, and 12 are not obvious as no motivation exists to combine the prior art elements in the manner presently claimed. Indeed, when considered as a whole, the references teach away from the claimed composition. Claims 1, 2, 7, and 12 are additionally not obvious as, absent hindsight, no reasonable expectation of success would have existed for combining the prior art in the manner claimed.

Claim 1 recites a composition containing human TGFα "hTGFα". The hTGFα comprises the amino acid sequence of SEQ ID NO 2. The composition contains hTGFα or a combination of hTGFα with other EGF-R ligands, coupled with a carrier protein P64k. The composition contains an adjuvant, and is able to produce a specific immune response against said hTGFα.

Hoeprich teaches a conjugate of human TGFα and limpet hemocyanine coupled using

gluteraldehyde.

Davila teaches vaccine compositions comprising autologous EGF for active immunization against the proliferation of EGF-dependent tumors, or other EGF-dependent diseases. The autologous EGF is coupled to a carrier protein such as tetanus toxoid, Cholera toxin B (CTB) chain, or P64. The vaccine compositions taught in Davila may include an adjuvant such as aluminum hydroxide.

Rodriquez discloses the identification of a nucleotide sequence which codes for a highly conserved protein and is common to the majority of pathogenic strains of *Neisseria* (named P64k). Rodriquez teaches the production of the protein with a high grade of purity and in commercially useful quantities, so that it can be employed in diagnostic methods and as an integrating part of a vaccine preparation of broad spectrum of protection.

The Office alleges that one of ordinary skill in the art would have been motivated to make a conjugate with hTGFα with P64k because the teachings of Davila show its successful use in a conjugate with EGF. Applicants respectfully disagree and note that when considering obviousness, the prior art must be considered as a whole including portions that would lead away from the claimed invention. *See, e.g.,* MPEP § 2141.02.

Applicants respectfully submit that upon considering Hoeprich, Davila, and Rodriquez, one of ordinary skill in the art would not be motivated to make a conjugate of hTGFα and P64k in accordance with the present claims. Davila teaches EGF conjugated to a laundry list of types of carrier proteins such as tetanus toxoid, Cholera toxin B (CTB) chain, or P64. As illustrated in Davila, the carrier protein CTB achieved the best results and is expressly preferred as a carrier protein with EGF. *See, e.g.,* Abstract, FIG. 2.

In Davila, comparing the experimental results obtained from CTB (*e.g.*, FIG. 2, col. 7, lines 15-20) and P64 (*e.g.*, FIG. 12, col. 11, lines 15-20) demonstrate that coupling EGF to CTB provides a better and a higher antibody titer. For example, at the 1:100 sera dilutions for P64 (FIG. 12), the majority of the mouse sera had an O.D. of 0.2 to 0.25, with a couple of sera at 0.5. *See* FIG. 12. CTB conjugates, at similar dilutions, resulted in an almost two fold increase in titer concentrations, ranging from approximately 0.3 to 0.8. *See* FIG. 2. Thus, Davila provides motivation for using CTB as a carrier protein rather than P64. Moreover, based on Davila, a person of ordinary skill in the art would not be motivated to use P64, as Davila teaches that CTB

provides the desired results.

Applicants additionally submit that claim 1, 2, 7, and 12 are not obvious as none of references relied upon by the Office teach or suggest that a combination of hTGFα and P64k would be effective in producing a specific immune response against hTGFα. It is understood in the art that the development of vaccines against a specific antigen target is a highly complex and specific process. Thus, while Davila may teach that P64 can be used with EGF, there is no reasonable expectation that hTGFα would be effective with P64 in eliciting a specific immune response. Indeed, Hoeprich suggests as much, stating that although TGFα and EGF share some sequence homology (33-40%), "their antibodies do not cross react, and they differ significantly in their occurrence." *See,* Hoeprich, page 19086, col. 2, 1st paragraph.

Applicants submit that claims 1, 2, 7, and 12 are not obvious because when the prior art is considered as a whole, no motivation exists to make the composition as presently claimed. Additionally, no reasonable expectation of success exists in modifying the cited references in accordance with the current claims. Accordingly, applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection.

Claims 1, 2, 4, 5, 7, 12, and 13 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoeprich (of record) in view of Davila (US Patent 5,894,018), in view of Rogdriquez et al. (US Patent 5,286,484), and in further view of Gonzalez 1997 (of record). Applicants respectfully traverse the rejection.

Applicants note the standard for obviousness and respectfully submit that the previous paragraphs demonstrate that Hoeprich, Davila, Rodriquez, and Gonzalez do not teach a composition comprising hTGFα or a combination of hTGFα with other EGF-R ligands, coupled with a carrier protein P64k. Additionally, no motivation exists and there is no reasonable expectation of success in modifying the references in accordance with the present claims. Accordingly, applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection.

Claims 1, 2, 4-7, 12, and 13 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hoeprich (of record) in view of Davila (US Patent 5,894,018), in view of Rogdriquez et al. (US Patent 5,286,484), and in further view of Ritzenthaler (Ritzenthaler, C. J.

General Virology, 76: 907-915, 1995). Applicants respectfully traverse the rejection.

Applicants note the standard for obviousness and respectfully submit that the previous paragraphs demonstrate that Hoeprich, Davila, Rodriquez, and Gonzalez do not teach a composition comprising hTGFα or a combination of hTGFα with other EGF-R ligands, coupled with a carrier protein P64k. Additionally, no motivation exists and there is no reasonable expectation of success in modifying the references in accordance with the present claims. Accordingly, applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection.

CONCLUSION

In light of the above amendments and remarks, the application should be in condition for allowance. If questions remain after consideration of the foregoing, or if the Office should determine that there are additional issues which might be resolved by a telephone conference, the Office is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,

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Enclosure: Petition for 3-month Extension of Time

Date: October 1, 2008
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